ALKOXYCARBONYLAMINO BENZOIC ACID OR ALKOXYCARBONYLAMINO TETRAZOLYL PHENYL DERIVATIVES AS IP ANTAGONISTS

Cross Reference to Related Inventions

This application claims benefit under Title 35 U.S.C. 119(e) of U.S. Provisional Applications Nos. 60/272,872 filed March 2, 2001, and 60/312,559 filed August 15, 2001, all applications are hereby incorporated by reference in its entirety.

Field of the Invention

This invention relates to certain alkoxycarbonylamino benzoic acid derivatives and alkoxycarbonylamino tetrazolyl phenyl derivatives, and associated pharmaceutical compositions, methods for use as prostaglandin IP (I_2, or PGI_2) antagonists, and methods of preparation thereof.

Background of the Invention

Prostaglandins or prostanoids (PGs) are a group of bioactive compounds derived from membrane phospholipids and are formed from 20-carbon essential fatty acids containing three, four, or five double bonds, and a cyclopentane ring. They fall into several main classes designated by the letters D, E, F, G, H, or I, and they are distinguished by substitutions to the cyclopentane ring. The main classes are further subdivided by subscripts 1, 2, or 3, which reflect their fatty acid precursors. Thus, PGI_2 has a double ring structure, and the subscript 2 indicates that it is related to arachidonic acid.

Prostaglandins are known to be generated locally in the bladder in response to physiologic stimuli such as stretch of the detrusor smooth muscle, injuries of the vesical mucosa, and nerve stimulation (K. Anderson, *Pharmacological Reviews* **1993**, 45(3), 253-308). PGI_2 (also known as prostacyclin) is the major prostaglandin released from the human bladder. There are some suggestions that prostaglandins may be the link between detrusor muscle stretch produced by bladder filling and activation of C-fiber afferents by bladder distension. It has been proposed that